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EXAMINER

HUTSON, RICHARD G

ART UNIT

PAPER NUMBER

1652

MAIL DATE

DELIVERY MODE

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PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

DETAILED ACTION

Applicant's amendment of claim 2 in the paper of 5/28/2008, is acknowledged.

Claims 2, 6-9, 14, 17, 20, 37-40, 69 and 71-75 remain present and at issue for examination.

Applicants' arguments filed on 5/28/2008, have been fully considered.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 6-9, 14, 17, 20, 37-40, 69 and 71-75 remain rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The rejection was stated in the previous office action as it applied to previous claims 2, 6-9, 14, 17, 20, 37-40, 69 and 71-75. In response to this rejection applicants have amended claim 2 and traverse the rejection as it applies to the newly amended claims.

Applicants traverse this rejection based upon a lack of written description and the rejection based upon a lack of enablement together. Applicants submit that the present

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claims relate to Pol I type *Thermatoga neapolitana* DNA polymerases having reduced or no misincorporation of nucleotides during nucleic acid synthesis with a modification in the O-helix region defined by SEQ ID NO. 1. Applicants submit that the claimed modification comprises an amino acid substitution at position Arg722 (*i.e.*, with Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, or Val) and an amino acid substitution at position Lys726 (*i.e.*, with Ala, Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Met, Phe, Pro, Ser, Thr, Trp, Tyr, or Val) or an amino acid substitution at position Arg722 (*i.e.*, with Ala, Asn, Asp, Cys, Gln, Glu, Gly, His, He, Leu, Lys, Met, Phe, Pro, Ser, Thr, Trp, Tyr, or Val) and an amino acid substitution at position Phe730 (*i.e.*, with Ala, Arg, Asn, Asp, Cys, Gln, Glu, Gly, His, Ile, Leu, Lys, Met, Pro, Ser, Thr, Trp, Tyr, or Val).

Applicants note that according to the Examiner Interview Summary dated May 15, 2008, the outstanding written description and enablement rejections under 112, first paragraph, are based "upon the use of the terminology "comprising a modification" for allegedly opening up the claimed genus of mutants "such that the genus was excessively broad, such that it was not enabled or described." See Examiner Interview Summary issued May 15, 2008.

Applicants submit that they disagree with this characterization, however, in an effort to expedite allowance and without acquiescing to the Examiner's assertions, Applicants submit that they have amended the language of claim 2. Applicants submit that the use of the terminology "comprising a modification" has been amended.

Applicants further submit that present claim 2 has also been amended to include features which read on the O-helix defined by SEQ ID NO. 1.

Applicants submit that support for the amendment may be found, for example, on page 19, lines 4-16 and page 5, lines 20-28 of the Specification and/or in the general knowledge of those skilled in the art. Applicants submit that thus based upon this amendment, the written description and enablement rejections with regard to the present claims are moot.

Applicant's amendment and complete argument is acknowledged and has been carefully considered, however, is found nonpersuasive on the following basis.

While it is noted that applicants have removed the use of the terminology "comprising a modification", applicants amendment simultaneously adds the term "comprising" which allows the issue upon which the rejections are based to remain. While previously applicant's claims read on a DNA polymerase "comprising a modification...", applicant's claims now read on a DNA polymerase "comprising...". Thus the interpreted "openness" of the claims remains as does the reason upon which the previous rejections were based.

Thus the previous rejection remains for the reasons made of record and repeated herein. It remains that there is no disclosure of any particular structure to function/activity relationship in the disclosed species, sufficient to describe additional mutations that reduce or eliminate misincorporation of nucleotides. The specification fails to describe additional representative species of these mutant polymerases by any

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identifying structural characteristics or properties other than the activities recited in claim 3, for which no predictability of structure is apparent. Given this lack of additional representative species as encompassed by the claims, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 2, 6-9, 14, 17, 20, 37-40, 69, 71-75 are further rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a Pol I type mutant The DNA polymerase wherein said The DNA polymerase consists of the specific amino acid modification of positions Arg 722 and Lys 726, does not reasonably provide enablement for any Pol I type mutant The DNA polymerase comprising a modification that reduces or eliminates misincorporation of nucleotides comprising positions Arg 722 and Lys 726 or Arg 722 and Phe 730. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

The rejection was stated in the previous office action as it applied to previous claims 2, 6-9, 14, 17, 20, 37-40, 69 and 71-75. In response to this rejection applicants

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have amended claim 2 and traverse the rejection as it applies to the newly amended claims.

As discussed above, applicants traverse this rejection together with the rejection based upon a lack of written description on the basis that the use of the terminology "comprising a modification" has been amended. Applicants further submit that present claim 2 has also been amended to include features which read on the O-helix defined by SEQ ID NO. 1.

Applicants submit that support for the amendment may be found, for example, on page 19, lines 4-16 and page 5, lines 20-28 of the Specification and/or in the general knowledge of those skilled in the art. Applicants submit that thus based upon this amendment, the written description and enablement rejections with regard to the present claims are moot.

Applicant's amendment and complete argument is acknowledged and has been carefully considered, however, is found nonpersuasive on the following basis.

As above, while it is noted that applicants have removed the use of the terminology "comprising a modification", applicants amendment simultaneously adds the term "comprising" which allows the issue upon which the rejections are based to remain. While previously applicant's claims read on a DNA polymerase "comprising a modification...", applicant's claims now read on a DNA polymerase "comprising...". Thus the interpreted "openness" of the claims remains as does the reason upon which the previous rejections were based.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any Pol I type mutant Tne DNA polymerase comprising a modification that reduces or eliminates misincorporation of nucleotides comprising positions Arg 722 and Lys 726 or Arg 722 and Phe 730 because the specification does not establish: (A) regions of the protein structure which may be modified without effecting polymerase, exonuclease and proofreading activity; (B) the general tolerance of Tne DNA polymerases to modification and extent of such tolerance; (C) a rational and predictable scheme for modifying any amino acid residue of a Tne DNA polymerase with an expectation of obtaining the desired biological function; and (D) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful. Because of this lack of guidance, the extended experimentation that would be required to determine which substitutions would be acceptable to retain the polymerase, exonuclease and proofreading activity desired and the fact that the relationship between the sequence of a peptide and its tertiary structure (i.e. its activity) are not well understood and are not predictable, it would require undue experimentation for one skilled in the art to arrive at the majority of those mutant DNA polymerases of the claimed genus having the reduced or eliminated misincorporation activity.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including any number of amino acid modifications of any Pol I type mutant Tne DNA polymerase comprising a modification that reduces or

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eliminates misincorporation of nucleotides comprising positions Arg 722 and Lys 726 or Arg 722 and Phe 730. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of those mutants having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Conclusion

THIS ACTION IS MADE FINAL. Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Richard G. Hutson whose telephone number is 571-272-0930. The examiner can normally be reached on M-F, 7:00-4:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Nashaat T. Nashed can be reached on 571-272-0934. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

rg
8/5/2008

/Richard G Hutson, Ph.D./
Primary Examiner, Art Unit 1652